Evaluation of Enzyme Testing for the Detection of Myocardial Infarction Following Direct Coronary Surgery

By Edwin L. Alderman, M.D., Harvey J. Matloff, M.D., Norman E. Shumway, M.D., and Donald C. Harrison, M.D.

SUMMARY
The serial measurement of postoperative serum enzymes has been proposed as an important method for identifying myocardial infarction following aorto-coronary graft surgery. Serum glutamic oxalacetic transaminase, creatine phosphokinase and lactic dehydrogenase levels were determined during the initial five days following direct coronary artery surgery in 112 patients. Enzyme test results were analyzed by frequency distribution plots. Twelve patients (10.7%) developed definite electrocardiographic evidence of myocardial infarction within two weeks of surgery, seven on the first postoperative day. A general correlation of higher serum enzyme values and electrocardiographic evidence for myocardial infarction was established. However, the use of arbitrarily selected 90th percentile enzyme levels yielded a substantial number of false-negative and false-positive results as compared with electrocardiographic diagnosis. The 90th percentile levels were substantially higher following multi-vessel surgery, compared with single-vessel surgery. Thus, analysis of serum enzymes following coronary surgery was found to be a useful, but not definitive adjunct in identifying patients suspect for operative infarction.

Additional Indexing Words:
Aorto-coronary bypass surgery
Serum glutamic oxalacetic transaminase
Creatine phosphokinase
Lactic dehydrogenase

Since the widespread application of surgical treatment for coronary artery disease, detection of intraoperative or early postoperative myocardial infarction has become critical for evaluating the postoperative response of patients. First, myocardial infarction would be expected to have a direct influence on surgical mortality and morbidity. Second, myocardial necrosis resulting from coronary surgery, which necessitates the temporary manipulation of the blood supply to ischemic myocardium, might itself be responsible for relief of angina. Last, myocardial damage during and after surgery will diminish myocardial function reserve, potentially contributing to cardiac disability.

Recent reports suggest that serial postoperative serum enzyme values may aid in identifying patients with postoperative infarction.1-3 The purpose of this study was to evaluate this hypothesis in a large series of patients undergoing direct coronary surgery.

Methods
One-hundred and twelve consecutive patients who had direct coronary surgery for angiographically proven arteriosclerotic disease comprised the study group. Patients who had associated aneurysmectomy, valve replacement, or ventricular plication were excluded, as were patients who did not survive surgery. Three other patients were excluded because of marked elevation of postoperative serum enzymes, due to acute tubular necrosis (two patients), and blood transfusion reaction with hemolysis (one patient). The mean age of these 112 patients was 52 years, with a male to female ratio of 7:1. Fifty-eight percent of the patients had prior myocardial infarctions by history or evidence on their electrocardiograms. Thirty-nine patients had surgery on a single coronary artery; 73 had surgery on two or more vessels, using multiple grafts, and 26 of these had concomitant right coronary artery endarterectomy.4 Aorto-coronary bypass surgery was performed in a manner similar to that described by Favaloro et al.5 Cardiopulmonary bypass was instituted with mild systemic hypothermia, usually to 34°C. Distal coronary perfusion and/or external cardiac cooling were not employed. The heart was electrically fibrillated, and in most patients a sump drain was placed through the left ventricular apex. The coronary artery was mobilized by use of elastic ligatures for end-to-side anastomosis of the
reversed saphenous vein autograft. The duration of distal coronary occlusion while the anastomosis was made ranged from 12-25 min.

On the morning of the first through the fifth postoperative days, a 12-lead electrocardiogram was recorded and a venous blood specimen was obtained. Additional cardiograms were obtained the day prior to hospital discharge (average duration of hospitalization was 10 days) and during subsequent clinical followup. All electrocardiograms were interpreted prior to any knowledge of serum enzyme levels. Blood was analyzed spectrophotometrically for serum glutamic oxalacetic transaminase (SGOT), creatine phosphokinase (CPK), and lactic dehydrogenase (LDH). An occasional SGOT determination was performed by the SMA-12/60 colorimetric method and was corrected for the temperature difference in the two methods. The upper limits of normal for enzyme testing in our laboratory are: SGOT-40 IU/liter, CPK (male)-90 IU/liter, CPK (female)-70 IU/liter, and LDH-200 IU/liter.

Results

Electrocardiographic Criteria

Serial postoperative electrocardiograms revealed a spectrum of alterations ranging from simple T wave changes to classic transmural infarction. Although strict criteria were employed for the electrocardiographic diagnosis of infarction, there were many patients with substantial degrees of electrocardiographic abnormality which made discrete separation difficult. Diagnosis of anterior or lateral infarction was made in five patients on the basis of the development of a classic transmural infarction pattern. The diagnosis of inferior infarction was based, in three patients, on significant widening and deepening of the Q wave to greater than one-third the height of the subsequent R wave, in association with evolving ST-T segment elevation. Four additional patients had the diagnosis of infarction, based on evolution of ST-T segment abnormalities, in association with loss of R wave amplitude occurring over several days.

Electrocardiographic changes diagnostic of myocardial infarction were initially noted on the first postoperative day in seven patients, and between the third and seventh postoperative day in five other patients (12/112-10.7%). Posthospitalization follow-up did not reveal any additional myocardial infarctions in the next 30 days. The 12 patients having infarction following direct coronary surgery did not differ from the entire group with respect to age, history of prior infarction and incidence of congestive heart failure. They did, however, all have multi-vessel coronary disease. Moreover, all seven of the intraoperative myocardial infarctions were in patients who had surgery on two or more vessels.

Enzyme Test Results

SGOT, LDH, and CPK results were analyzed separately for the 39 patients who had single vessel surgery and for the 73 patients who had multi-vessel surgery with or without endarterectomy. The enzyme test results of the endarterectomy patients were sufficiently similar in distribution to the multi-vessel surgery patients to form a combined group. The enzyme test results are illustrated in the form of frequency distributions for the first four postoperative days. Separate frequency distributions are shown for each enzyme and for each

![Graph](image-url)

Figure 1

The frequency distribution of SGOT results for the first through fourth postoperative days in patients who had multi-vessel surgery is illustrated. Patients with definite intraoperative myocardial infarction are plotted as solid squares and are not incorporated in the frequency distribution of the remaining patients. The arrows and adjacent enzyme values indicate the 90th percentile levels.
surgical group (figs. 1-4). All frequency distributions, irrespective of the enzyme type or the surgical procedure, demonstrated a positive skew distribution. The skew tended to be greater for the multi-vessel surgical group than the single-vessel surgical group. Moreover, the enzyme test results tended to display a long positive tail on the initial postoperative day, with progressive shortening on each subsequent day.

The 90th percentile level was approximated for each frequency distribution, the results of which are indicated by arrows on figures 1-4, and are summarized in table 1. The 90th percentile value for all three enzyme test results fell rapidly from a peak on the first postoperative day, generally reaching a plateau by the fourth postoperative day.

![Figure 2](image)

The frequency distribution of CPK test results is illustrated for the first through fourth postoperative days in patients who had multi-vessel surgery. The enzyme test results of those patients who had intraoperative myocardial infarction and the 90th percentile levels are indicated in the same manner as in figure 1.

![Figure 3](image)

The frequency distribution of LDH enzyme test results is illustrated for the first through fourth postoperative days in patients who had multi-vessel surgery. The enzyme test results of those patients who had intraoperative myocardial infarction and the 90th percentile levels are illustrated in the same manner as in figure 1.

<table>
<thead>
<tr>
<th>Table 1</th>
<th>90th Percentile Levels for Frequency Distribution of Enzyme Test Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Postoperative day</td>
<td>SGOT (IU/liter)</td>
</tr>
<tr>
<td></td>
<td>Single vessel</td>
</tr>
<tr>
<td>1</td>
<td>76</td>
</tr>
<tr>
<td>2</td>
<td>45</td>
</tr>
<tr>
<td>3</td>
<td>60</td>
</tr>
<tr>
<td>4</td>
<td>66</td>
</tr>
<tr>
<td>5</td>
<td>68</td>
</tr>
</tbody>
</table>
Substantial differences in the 90th percentile levels were noted between the single-vessel surgical group and the multi-vessel surgical group.

The enzyme test results of the seven patients who had definite intraoperative myocardial infarctions are illustrated in relation to the frequency distributions for the multi-vessel surgical group (figs. 1-3). Five of the seven intraoperative infarctions were associated with SGOT and CPK elevations in excess of the 90th percentile value on the first postoperative day, whereas by the third postoperative day only three of the seven patients’ SGOT exceeded the 90th percentile level. In contrast, the 90th percentile levels of the LDH frequency distributions yielded the best separation on the third postoperative day, at which time six of the seven patients with definite intraoperative infarction exceeded that LDH value.

The five patients who had suffered a myocardial infarction during the early postoperative period generally had a normal pattern of enzyme test results immediately postoperatively, with a late rise at the time of infarction. Enzyme data were incomplete for some of these patients because blood collection procedures had been terminated prior to the onset of infarction. The contrast between the postoperative enzyme pattern of a patient who had intraoperative infarction with the enzyme pattern resulting from an infarction occurring several days later during the recovery period is illustrated in figure 5.

Clinical and Angiographic Sequelae

Graft patency data were available in 9 of the 12 patients having intraoperative or early postoperative infarction, either by postmortem examination or from angiographic restudy. Twelve of 18 grafts in this patient group were occluded (67%), two were stenotic, and four were patent. Eight of the nine patients in whom patency data were available had occluded grafts to coronary arteries, with myocardial distribution patterns coinciding with the infarct location suggested by the electrocardiogram.

Figure 4

The frequency distributions of SGOT, CPK, and LDH enzyme test results are illustrated for postoperative days 1 through 4 in those patients having single vessel coronary surgery. The arrows and adjacent numbers indicate the 90th percentile levels for each frequency distribution.

Figure 5

The enzyme test results for two individual patients are illustrated. Patient V.B. had a definite intraoperative myocardial infarction with SGOT test results for the first two postoperative days exceeding the 90th percentile level for patients undergoing multi-vessel surgery. In contrast, patient H.O. had an early postoperative infarction with SGOT test results for the fourth and fifth postoperative days exceeding the 90th percentile level.
The follow-up of those patients without electrocardiographic evidence of infarction but with enzyme test results at the upper end of the frequency distributions are of particular interest. An analysis of the clinical course of these patients did not demonstrate a different incidence of postoperative heart failure from those patients in the lower percentile. Moreover, the mean change in ejection fraction of those patients evaluated one year postoperatively and who exceeded the 75th percentile level was not significantly different from the mean change in patients who were below the 25th percentile level (mean change in ejection fraction of the 75th percentile: +0.04, N = 6; mean change in ejection fraction of the 25th percentile: +0.01, N = 7).

Discussion

In this study, the frequency distributions of postoperative enzyme test results were clearly asymmetrical, as are frequency distributions of enzyme results (SGOT) in normal subjects.\textsuperscript{10, 11} The use of an upper limit percentile enzyme level as an index for the identification of patients who are suspect for myocardial damage seems more appropriate than the use of arbitrary indices or indices based on a normal distribution analysis.\textsuperscript{12} However, in our study it was apparent that the enzyme test results did not provide a dichotomous separation between patients demonstrating myocardial infarction and those who did not. Using the 90th percentile SGOT threshold level of 140 as an arbitrary index, only 5 of 11 patients exceeding this value had a definite myocardial infarction. Although arbitrary enzyme values have been reported to provide some separation between patients with infarction versus those without, the data from these reports are similarly nondichotomous. Electrocardiographic confirmation of infarction was noted in patients with an SGOT above 90 IU/liter in 11 of 16 cases by Hultgren et al.,\textsuperscript{1} and in patients with an SGOT over 100 IU/liter in 5 of 8 cases by Greenberg et al.\textsuperscript{2} and in 7 of 11 cases by Dietrich et al.\textsuperscript{3} Most of the patients reported in these studies had myocardial implantation procedures, rather than saphenous vein bypass procedures.

Despite the failure of an index enzyme level to provide a precise identification of patients with myocardial infarction, the observation of enzyme test results at the upper end of a frequency distribution for a particular surgical procedure does raise the question of myocardial damage. In support of this concept there was a spectrum of abnormal electrocardiographic patterns which, although nondiagnostic for infarction, nevertheless correlated to a reasonable extent with enzyme test results. An argument against this conclusion, however, is the fact that the postoperative course of patients with elevated enzyme results was not different from that of patients with low enzyme results. Moreover, postoperative ejection fractions were not significantly affected in a small number of patients who have been restudied to date.

There are clearly many factors contributing to enzyme elevations following cardiac surgery. In patients undergoing multi-vessel surgery, the median first day SGOT level was twice preoperative levels, and the CPK median levels were four times preoperative levels. The extreme variability of the enzyme response to intraoperative and postoperative factors make it unlikely that a discrete distinction can be made between surgery with or without infarction. Since during the course of coronary surgery both cardiac and non-cardiac tissues are manipulated, it would be desirable to utilize isoenzyme determinations specific for cardiac muscle. Such determinations, which were not performed in this study, utilize the CPK-MB isoenzyme and according to initial reports, provide a substantially greater degree of myocardial specificity than CPK alone.\textsuperscript{12, 14}

Caution should be exercised in the extrapolation of these enzyme test results to the experience of other medical centers. All enzyme tests in this study were determined spectrophotometrically, which yields somewhat lower levels than colorimetric determinations that are usually performed in automated screening tests.\textsuperscript{9} Moreover, the colorimetric determination tends to be artificially elevated by such drugs as erythromycin, oxacillin and others which may be employed in the postoperative patient.\textsuperscript{15} In addition, the particular surgical procedure employed for direct coronary surgery will have considerable impact upon the distribution of enzyme results. In this study, enzyme test results were very different between patients undergoing single vessel surgery and multi-vessel surgery. Technical factors such as the method of inducing cardiac arrest, coronary perfusion, aortic cross-clamping and others may be expected to influence enzyme test results. In view of the multiplicity of these factors, it is probable that each institution would have to establish its own enzyme frequency distribution in postoperative patients. While measurement of serial serum enzymes is generally helpful after saphenous vein coronary
artery operations, changes in these alone cannot reliably identify patients with intraoperative infarction.

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EDWIN L. ALDERMAN, HARVEY J. MATLOF, NORMAN E. SHUMWAY and DONALD C. HARRISON

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